

CLAIMS

1. An isolated nucleic acid molecule selected from the group consisting of
(a) a nucleic acid molecule which codes for a RUR-1 sense-encoded or a RUR-1 antisense-encoded polypeptide and which hybridizes under stringent conditions to a molecule having a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO:1 and the nucleotide sequence of SEQ ID NO:4,
(b) deletions, additions and substitutions of the nucleic acid molecules of (a), which code for a a RUR-1 sense-encoded or a RUR-1 antisense-encoded polypeptide,
(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
(d) complements of (a), (b) and (c).
2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.
3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the coding region of the nucleotide sequence of SEQ ID NO:1.
4. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO:1.
5. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:4.
6. The isolated nucleic acid molecule of claim 1 wherein the isolated nucleic acid molecule comprises the coding region of the nucleic acid sequence of SEQ ID NO:4.
7. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO:4.
8. An isolated nucleic acid molecule selected from the group consisting of:
(a) a unique fragment of nucleotides 1-1382 of SEQ ID NO:1 between 12 and 1381

contiguous nucleotides in length,

(b) a unique fragment of nucleotides 12167 of SEQ ID NO:4 between 12 and 2166 contiguous nucleotides in length,

(c) complements of "(a)", and

(d) complements of "(b)",

wherein the unique fragment excludes nucleic acid molecules which consist only of a nucleotide sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:11.

9. The isolated nucleic acid molecule of claim 8, wherein the isolated nucleic acid molecule is selected from the group consisting of nucleic acid molecules having at least 14 contiguous nucleotides, 15 contiguous nucleotides, 16 contiguous nucleotides, 18 contiguous nucleotides, 20 contiguous nucleotides, 22 contiguous nucleotides and 25 contiguous nucleotides.

10. The isolated nucleic acid molecule of claim 8, wherein the isolated nucleic acid molecule is between 12 and 32 contiguous nucleotides.

11. The isolated nucleic acid molecule of claim 8, wherein the isolated nucleic acid molecule comprises at least 5 contiguous nucleotides not present in SEQ ID NO:10 or SEQ ID NO:11.

12. An expression vector comprising the isolated nucleic acid molecule of any of claims 1-11 operably linked to a promoter.

13. A host cell transformed or transfected with the expression vector of claim 12.

14. The host cell of claim 13, wherein the host cell expresses an HLA molecule.

15. An isolated polypeptide encoded by the isolated nucleic acid molecule of any of claims 1-7, or a functional variant thereof having additions, deletions or substitutions in the amino acid sequence of the isolated polypeptide.

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A4

16. The isolated polypeptide of claim 15, wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence of SEQ ID NO:2, the amino acid sequence of SEQ ID NO:3 and the amino acid sequence of SEQ ID NO:5.

Sub A57 5 17. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:3.

Sub E1 10 18. An isolated polypeptide selected from the group consisting of:

(a) a unique fragment of SEQ ID NO:2 between 9 and 83 amino acids in length, and

(b) a unique fragment of SEQ ID NO:5 between 9 and 475 amino acids in length.

19. The isolated polypeptide of claim 18, wherein the unique fragment binds to a polypeptide-binding agent.

20. The isolated polypeptide of claim 19, wherein the polypeptide-binding agent is an antibody or a cytotoxic T lymphocyte.

21. An isolated polypeptide which selectively binds a protein encoded by the isolated nucleic acid molecule of any of claims 1-7.

22. The isolated polypeptide of claim 21, wherein the isolated polypeptide is an Fab or F(ab)₂ fragment of an antibody.

23. The isolated polypeptide of claim 21, wherein the isolated polypeptide is a fragment of an antibody, the fragment including a CDR3 region selective for the protein.

24. The isolated polypeptide of claim 21, wherein the isolated polypeptide is a monoclonal antibody.

Sub E1 30 25. A kit for detecting the presence of the expression of a nucleic acid which encodes a tumor associated polypeptide precursor, comprising a pair of isolated nucleic acid molecules each of which consists of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of nucleotides 1-1382 of SEQ ID NO:1, and (b) complements

of "(a)", wherein the contiguous segments are nonoverlapping.

26. The kit of claim 25, a wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

27. The kit of claim 26, wherein the pair of isolated nucleic acid molecules is SEQ ID NO:8 and SEQ ID NO:9.

28. The kit of claim 25 wherein the pair of isolated nucleic acid molecules is PCR primers, wherein one of the primers is a unique fragment of SEQ ID NO:1.

29. A method for diagnosing a disorder characterized by expression of a RUR-1 antisense cDNA nucleic acid molecule or an expression product thereof, comprising:

contacting a biological sample isolated from a subject with an agent that selectively binds the isolated RUR-1 antisense cDNA nucleic acid molecule of claim 1 or an expression product thereof, and

determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

30. The method of claim 29 wherein the agent is a nucleic acid molecule comprising SEQ ID NO:1 or a unique fragment thereof.

31. The method of claim 29 wherein the interaction is determined by amplifying at least a portion of the nucleic acid molecule.

32. The method of claim 29 wherein the agent is a cytolytic T lymphocyte.

33. The method of claim 29 wherein the agent is an antibody or antibody fragment.

34. The method of claim 29 wherein the biological sample is isolated from a tissue selected from the group consisting of non-liver tissue, non-kidney tissue, non-bladder tissue,

and non-testis tissue.

35. A method for treating a subject with a disorder characterized by expression of a RUR-1 antisense cDNA-encoded tumor associated polypeptide, comprising
administering to the subject an amount of an agent which enriches selectively in the subject the presence of complexes of a HLA molecule and a tumor rejection antigen derived from a RUR-1 antisense cDNA-encoded tumor associated polypeptide, sufficient to ameliorate the disorder.

36. The method of claim 35, wherein the agent is an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:3, or an immunogenic fragment thereof.

37. The method of claim 35, wherein the disorder is cancer excluding cancers selected from the group consisting of liver cancer, kidney cancer, bladder cancer, and testicular cancer.

38. A method for treating a subject with a disorder characterized by expression of a RUR-1 antisense cDNA nucleic acid molecule or an expression product thereof, comprising:
administering to the subject an amount of autologous cytotoxic T cells sufficient to ameliorate the disorder, wherein the cytotoxic T cells are specific for complexes of an HLA molecule and a RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

39. The method of claim 38, wherein the RUR-1 antisense cDNA-encoded tumor associated polypeptide comprises the amino acid sequence of SEQ ID NO:3.

40. The method of claim 39, wherein the disorder is cancer excluding cancers selected from the group consisting of liver cancer, kidney cancer, bladder cancer, and testicular cancer.

41. A method for treating a subject with a disorder characterized by expression of a RUR-1 antisense cDNA nucleic acid molecule or an expression product thereof, comprising:
administering to the subject an amount of a RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof sufficient to ameliorate the

disorder.

42. The method of claim 41, wherein the RUR-1 antisense cDNA-encoded tumor associated polypeptide comprises the amino acid sequence of SEQ ID NO:3.

43. The method of claim 42, wherein the disorder is cancer excluding cancers selected from the group consisting of liver cancer, kidney cancer, bladder cancer, and testicular cancer.

44. A method for enriching selectively a population of T cells with cytotoxic T cells specific for a RUR-1 antisense cDNA-encoded tumor associated polypeptide comprising:
contacting an isolated population of T cells with an agent presenting a complex of a RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof and a HLA presenting molecule in an amount sufficient to selectively enrich the isolated population of T cells with the cytotoxic T cells.

45. The method of claim 44 wherein the RUR-1 antisense cDNA-encoded tumor associated polypeptide comprises the amino acid sequence of SEQ ID NO:3.

46. The method of claim 45 wherein the agent is a cell which expresses a RUR-1 antisense cDNA-encoded tumor associated polypeptide and a HLA molecule.

47. A vaccine composition comprising a nucleic acid encoding a RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

48. The vaccine composition of claim 47, further comprising a nucleic acid encoding a second tumor associated polypeptide or an immunogenic fragment thereof which is a non-RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

49. A vaccine composition comprising a RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

50. The vaccine composition of claim 49, wherein the RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof comprises the amino acid sequence of SEQ ID NO:3.

51. The vaccine composition of claim 49, further comprising a second tumor associated polypeptide or an immunogenic fragment thereof which is a non-RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

52. A vaccine composition comprising a cell which expresses a RUR-1 antisense cDNA nucleic acid or polypeptide, or an immunogenic fragment thereof.

53. The vaccine composition of claim 52, the cell further comprising a second tumor associated nucleic acid or polypeptide, or an immunogenic fragment thereof, which is a non-RUR-1 antisense cDNA nucleic acid or tumor associated polypeptide, or an immunogenic fragment thereof.

54. The vaccine composition of any of claims 47-53, further comprising an adjuvant.

55. The vaccine composition of any of claims 47-53, further comprising a pharmaceutically acceptable carrier.

56. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:3, or an immunogenic fragment thereof.

57. The isolated nucleic acid molecule of claim 56, further comprising a nucleotide sequence encoding a second tumor associated polypeptide or an immunogenic fragment thereof which is a non-RUR-1 antisense cDNA-encoded tumor associated polypeptide or an immunogenic fragment thereof.

58. A composition comprising:
the isolated nucleic acid as claimed in claim 1 and

a pharmaceutically acceptable carrier.

59. A composition comprising:
the isolated polypeptide as claimed in claim 15, and
a pharmaceutically acceptable carrier.

60. A method for determining the prognosis of a disorder characterized by expression of a
RUR-1 antisense nucleic acid molecule or an expression product thereof, comprising:

(a) contacting a biological sample isolated from a subject at a first time with an agent
that selectively binds the isolated RUR-1 antisense nucleic acid molecule of claim 1 or an
expression product thereof,

(b) determining the interaction between the agent and the nucleic acid molecule or the
expression product as a determination of the state of the disorder at the first time,

(c) contacting a second biological sample isolated from the subject at a second time
with the agent,

(d) determining the interaction between the agent and the nucleic acid molecule or the
expression product in the second biological sample as a determination of the state of the
disorder at the second time, and

(e) comparing the state of the disorder at the first time and the second time as a
determination of the prognosis.

61. The method of claim 60 wherein the agent is a nucleic acid molecule comprising
SEQ ID NO:1 or a unique fragment thereof.

62. The method of claim 60 wherein the interactions are determined by amplifying at least
a portion of the nucleic acid molecule.

63. The method of claim 60 wherein the agent is a cytolytic T lymphocyte.

64. The method of claim 60 wherein the agent is an antibody or antibody fragment.

65. The method of claim 60 wherein the biological samples are isolated from a tissue

selected from the group consisting of non-liver tissue, non-kidney tissue, non-bladder tissue, and non-testis tissue.

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